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| FORM PTO-1449<br><br><u>INFORMATION DISCLOSURE STATEMENT</u> |  | ATTY. DOCKET NO.<br>0942.4110002/RWE/GER | APPLICATION NO.<br>09/028,514 |
|  |  | APPLICANT<br>Gorfien et al.              |                               |
|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643<br>165)         |

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| EXAMINER INITIAL |     | DOCUMENT NUMBER | DATE       | NAME        | CLASS | SUB-CLASS | FILING DATE |
|------------------|-----|-----------------|------------|-------------|-------|-----------|-------------|
| JKW              | AA1 | 4,673,649       | 06/16/1987 | Boyce       | 435   | 240       | 07/15/1983  |
| JKW              | AB1 | 4,767,704       | 08/30/1988 | Cleveland   | 435   | 68        | 10/07/1983  |
| JKW              | AC1 | 4,927,762       | 05/22/1990 | Darfler     | 435   | 240.31    | 11/30/1988  |
| JKW              | AD1 | 4,940,666       | 07/10/1990 | Boyce       | 435   | 240.2     | 12/09/1986  |
| JKW              | AE1 | 4,959,319       | 09/25/1990 | Skelnik     | 435   | 240.2     | 02/17/1989  |
| JKW              | AF1 | 5,024,947       | 06/18/1991 | Inlow       | 435   | 240.31    | 07/24/1987  |
| JKW              | AG1 | 5,045,454       | 09/03/1991 | Bertheussen | 435   | 29        | 02/23/1990  |
| JKW              | AH1 | 5,063,157       | 11/05/1991 | Stockinger  | 435   | 240.2     | 01/11/1989  |
| JKW              | AI1 | 5,089,397       | 02/18/1992 | Kushner     | 435   | 69.1      | 06/14/1989  |
| JKW              | AJ1 | 5,122,469       | 06/16/1992 | Mather      | 435   | 240.2     | 10/03/1990  |
| JKW              | AK1 | 5,166,066       | 11/24/1992 | Carter      | 435   | 240.2     | 07/11/1991  |
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| EXAMINER INITIAL |     | DOCUMENT NUMBER | DATE       | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|------------------|-----|-----------------|------------|---------|-------|-----------|-------------|
| JKW              | AL1 | WO 86/04290     | 08/28/1986 | WIPO    | —     | —         | Yes<br>No   |
| JKW              | AM1 | EP 0 441 695 B1 | 08/14/1991 | Europe  | —     | —         | Yes<br>No   |
| JKW              | AN1 | WO 92/05246     | 04/02/1992 | WIPO    | —     | —         | Yes<br>No   |
| JKW              | AO1 | 0 481 791 A2    | 04/22/1992 | Europe  | —     | —         | Yes<br>No   |
| JKW              | AP1 | WO 96/14395     | 05/17/1996 | WIPO    | —     | —         | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|     |    |   |   |
|-----|----|---|---|
| JKW | AR | 1 | "Serum-Free Media, Method for Culturing Animal Cells, and Process for Producing Physiologically Active Substances," PCT Gazette No. 01/1998, p. 275 (January 8, 1998) |
| JKW | AS | 1 | JRH Biosciences Catalog No. 14602, 8 pages (1993)   |
| JKW | AT | 1 | Battista, P.J. et al., "Serum-free media for the culture of Chinese hamster ovary cells," American Biotechnology Laboratory 12:64-68 (April 1994)                     |

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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

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|  |  | APPLICANT<br>Gorfien et al.              |  |                               |  |
|  |  | FILING DATE<br>February 23, 1998         |  | GROUP<br>1643                 |  |

## U.S. PATENT DOCUMENTS

| EXAMINER INITIAL |     | DOCUMENT NUMBER | DATE       | NAME      | CLASS | SUB-CLASS | FILING DATE |
|------------------|-----|-----------------|------------|-----------|-------|-----------|-------------|
| <i>JKW</i>       | AA2 | 5,316,938       | 05/31/1994 | Keen      | 435   | 240.31    | 12/18/1992  |
| <i>JKW</i>       | AB2 | 5,318,898       | 06/07/1994 | Israel    | 435   | 69.1      | 04/02/1991  |
| <i>JKW</i>       | AC2 | 5,342,777       | 08/30/1994 | Cole      | 435   | 240.31    | 03/03/1992  |
| <i>JKW</i>       | AD2 | 5,378,612       | 01/03/1995 | Nakashima | 435   | 69.6      | 12/28/1992  |
| <i>JKW</i>       | AE2 | 5,405,772       | 04/11/1995 | Ponting   | 435   | 240.31    | 06/18/1993  |
| <i>JKW</i>       | AF2 | 5,422,250       | 06/06/1995 | Mignot    | 435   | 69.6      | 11/03/1992  |
| <i>JKW</i>       | AG2 | 5,443,968       | 08/22/1995 | Takazawa  | 435   | 70.3      | 04/30/1993  |
| <i>JKW</i>       | AH2 | 5,474,931       | 12/12/1995 | DiSorbo   | 435   | 240.31    | 09/21/1993  |
| <i>JKW</i>       | AI2 | 5,516,654       | 05/14/1996 | Israel    | 435   | 69.1      | 01/27/1994  |
| <i>JKW</i>       | AJ2 | 5,573,937       | 11/12/1996 | Shinmoto  | 435   | 240.1     | 01/09/1995  |
| <i>JKW</i>       | AK2 | 5,576,194       | 11/19/1996 | Chan      | 435   | 69.6      | 10/01/1993  |
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| EXAMINER INITIAL |     | DOCUMENT NUMBER | DATE       | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|------------------|-----|-----------------|------------|---------|-------|-----------|-------------|
| <i>JKW</i>       | AL2 | WO 96/39487     | 12/12/1996 | WIPO    | —     | —         | Yes<br>No   |
|                  | AM  |                 |            |         |       |           | Yes<br>No   |
|                  | AN  |                 |            |         |       |           | Yes<br>No   |
|                  | AO  |                 |            |         |       |           | Yes<br>No   |
|                  | AP  |                 |            |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|            |    |   |  |
|------------|----|---|--|
| <i>JKW</i> | AR | 2 | Bebbington, C.R., "The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells," <i>DNA Cloning Volume III. A Practical Approach</i> , D.M. Glover, ed., IRL Press, publ., pp. 163-188 (1987) |
| <i>JKW</i> | AS | 2 | Berg, D.T. et al., "High-Level Expression of Secreted Proteins from Cells Adapted to Serum-Free Suspension Culture," <i>BioTechniques</i> 14:972-978 (1993)  |
| <i>JKW</i> | AT | 2 | Chaproniere-Rickenberg, D.M. & Webber, M.M., "Zinc Levels in Zinc-Stabilized Insulin are Inhibitory to the Growth of Cells in Vitro," <i>In Vitro</i> 19:373-375 (May 1983)  |

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*Deborah K. Wob*

DATE CONSIDERED

12-6-99

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| FORM PTO-1449<br><u>INFORMATION DISCLOSURE STATEMENT</u> |  | ATTY. DOCKET NO.<br>0942.4110002/RWE/GER |  | APPLICATION NO.<br>09/028,514 |  |
|  |  | APPLICANT<br>Gorfien et al.              |  |                               |  |
|  |  | FILING DATE<br>February 23, 1998         |  | GROUP<br>1643                 |  |

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| EXAMINER INITIAL |     | DOCUMENT NUMBER | DATE       | NAME     | CLASS | SUB-CLASS | FILING DATE |
|------------------|-----|-----------------|------------|----------|-------|-----------|-------------|
| <i>Dee</i>       | AA3 | 5,631,159       | 05/20/1997 | Marshall | 435   | 383       | 09/22/1993  |
| <i>Dee</i>       | AB3 | 5,633,162       | 05/27/1997 | Keen     | 435   | 384       | 03/04/1994  |
| <i>Dee</i>       | AC3 | 5,641,647       | 06/24/1997 | Fischer  | 435   | 69.1      | 08/24/1993  |
| <i>Dee</i>       | AD3 | 5,707,832       | 01/13/1998 | Mignot   | 435   | 69.6      | 02/07/1995  |
|                  | AE  |                 |            |          |       |           |             |
|                  | AF  |                 |            |          |       |           |             |
|                  | AG  |                 |            |          |       |           |             |
|                  | AH  |                 |            |          |       |           |             |
|                  | AI  |                 |            |          |       |           |             |
|                  | AJ  |                 |            |          |       |           |             |
|                  | AK  |                 |            |          |       |           |             |

## FOREIGN PATENT DOCUMENTS

| EXAMINER INITIAL |    | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|------------------|----|-----------------|------|---------|-------|-----------|-------------|
|                  | AL |                 |      |         |       |           | Yes<br>No   |
|                  | AM |                 |      |         |       |           | Yes<br>No   |
|                  | AN |                 |      |         |       |           | Yes<br>No   |
|                  | AO |                 |      |         |       |           | Yes<br>No   |
|                  | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|            |    |   |  |
|------------|----|---|--|
| <i>Dee</i> | AR | 3 | Freshney, R.I., "Culture of Animal Cells," A Manual of Basic Technique, Alan R. Liss, Inc., publ., New York, pp. 80-81 (1987)                                      |
| <i>Dee</i> | AS | 3 | Garnier, A. et al., "Scale-up of the adenovirus expression system for the production of recombinant protein in human 293S cells," Cytotechnology 15:145-155 (1994) |
| <i>Dee</i> | AT | 3 | Gramer, M.J. and Goochee, C.F., "Glycosidase Activities in Chinese Hamster Ovary Cell Lysate and Cell Culture Supernatant," Biotechnol. Prog. 9:366-373 (1993)     |

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*D. L. L. & W.*

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12-6-99

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|  |  | APPLICANT<br>Gorfien et al.              |  |                               |  |
|  |  | FILING DATE<br>February 23, 1998         |  | GROUP<br>1643<br><i>(165)</i> |  |

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| EXAMINER<br>INITIAL |    | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|---------------------|----|-----------------|------|------|-------|-----------|-------------|
|                     | AA |                 |      |      |       |           |             |
|                     | AB |                 |      |      |       |           |             |
|                     | AC |                 |      |      |       |           |             |
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|                     | AF |                 |      |      |       |           |             |
|                     | AG |                 |      |      |       |           |             |
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|                     | AJ |                 |      |      |       |           |             |
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## FOREIGN PATENT DOCUMENTS

| EXAMINER<br>INITIAL |    | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
|                     | AL |                 |      |         |       |           | Yes<br>No   |
|                     | AM |                 |      |         |       |           | Yes<br>No   |
|                     | AN |                 |      |         |       |           | Yes<br>No   |
|                     | AO |                 |      |         |       |           | Yes<br>No   |
|                     | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|            |    |   |  |
|------------|----|---|--|
| <i>Dku</i> | AR | 4 | Gramer, M.J. and Goochee, C.F., "Glycosidase Activities of the 293 and NS0 Cell Lines, and of an Antibody-Producing Hybridoma Cell Line," <i>Biotechnology and Bioengineering</i> 43(5):423-428 (March 1994) |
| <i>Dku</i> | AS | 4 | Gramer, M.J. et al., "Removal of Sialic Acid from a Glycoprotein in CHO Cell Culture Supernatant by Action of an Extracellular CHO Cell Sialidase," <i>Biotechnology</i> 13:692-698 (July 1995)              |
| <i>Dku</i> | AT | 4 | Hall, C.V. et al., "Expression and Regulation of <i>Escherichia coli</i> lacZ Gene Fusions in Mammalian Cells," <i>Journal of Molecular and Applied Genetics</i> 2(1):101-109 (1983)                         |

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*Deborah K. Abu*

DATE CONSIDERED

12-6-95

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|  |  | APPLICANT<br>Gorfien et al.              |                               |
|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643<br><i>(65)</i>  |

| U.S. PATENT DOCUMENTS |    |                 |      |      |       |           |             |
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| EXAMINER<br>INITIAL   |    | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|                       | AA |                 |      |      |       |           |             |
|                       | AB |                 |      |      |       |           |             |
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|                       | AD |                 |      |      |       |           |             |
|                       | AF |                 |      |      |       |           |             |
|                       | AF |                 |      |      |       |           |             |
|                       | AG |                 |      |      |       |           |             |
|                       | AH |                 |      |      |       |           |             |
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|                       | AJ |                 |      |      |       |           |             |
|                       | AK |                 |      |      |       |           |             |

| FOREIGN PATENT DOCUMENTS |    |                 |      |         |       |           |             |
|--------------------------|----|-----------------|------|---------|-------|-----------|-------------|
| EXAMINER<br>INITIAL      |    | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|                          | AL |                 |      |         |       |           | Yes<br>No   |
|                          | AM |                 |      |         |       |           | Yes<br>No   |
|                          | AN |                 |      |         |       |           | Yes<br>No   |
|                          | AO |                 |      |         |       |           | Yes<br>No   |
|                          | AP |                 |      |         |       |           | Yes<br>No   |

| OTHER (Including Author, Title, Date, Pertinent Pages, etc.) |    |   |   |  |  |  |  |
|--|----|---|---|--|--|--|--|
| <i>Skew</i>  | AR | 5 | Ham, R.G., "Clonal Growth of Mammalian Cells in a Chemically Defined, Synthetic Medium," Proc. N.A.S. 53:288-293 (February 1965)  |  |  |  |  |
| <i>Skew</i>  | AS | 5 | Ham, R.G., "Formulation of Basal Nutrient Media," Methods for Preparation of Media, Supplements, and Substrata for Serum-Free Animal Cell Culture, Alan R. Liss, Inc., publ., New York, pp. 3-21 (1984) |  |  |  |  |
| <i>Skew</i>  | AT | 5 | Hamilton, W.G. and Ham, R.G., "Clonal Growth of Chinese Hamster Cell Lines in Protein-Free Media," In Vitro 13:537-547 (September 1977)   |  |  |  |  |

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| EXAMINER<br><i>Deborah K. Weber</i>  | DATE CONSIDERED<br><i>102-6-99</i> |
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|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643<br>165)         |

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|                  | AA |                 |      |      |       |           |             |
|                  | AB |                 |      |      |       |           |             |
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|                  | AE |                 |      |      |       |           |             |
|                  | AF |                 |      |      |       |           |             |
|                  | AG |                 |      |      |       |           |             |
|                  | AH |                 |      |      |       |           |             |
|                  | AI |                 |      |      |       |           |             |
|                  | AJ |                 |      |      |       |           |             |
|                  | AK |                 |      |      |       |           |             |

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|                  | AL |                 |      |         |       |           | Yes<br>No   |
|                  | AM |                 |      |         |       |           | Yes<br>No   |
|                  | AN |                 |      |         |       |           | Yes<br>No   |
|                  | AO |                 |      |         |       |           | Yes<br>No   |
|                  | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|            |    |   |   |
|------------|----|---|---|
| <i>dkw</i> | AR | 6 | Kao, F-T. and Puck, T.T., "Genetics of Somatic Mammalian Cells, VII. Induction and Isolation of Nutritional Mutants in Chinese Hamster Cells," <i>Proc. N.A.S.</i> 60:1275-1281 (August 1968) |
| <i>dkw</i> | AS | 6 | Kyung, Y-S. et al., "High density culture of mammalian cells with dynamic perfusion based on on-line oxygen uptake rate measurements," <i>Cytotechnology</i> 14:183-190 (1994)                |
| <i>dkw</i> | AT | 6 | Lambert, K.J. and Birch, J.R., "Cell Growth Media," <i>Animal Cell Biotechnology</i> , Volume 1, R.E. Spier and J.B. Griffiths, eds. Academic Press, publ., pp. 85-122 (1985)                 |

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| EXAMINER | <i>Delph K. Ware</i> | DATE CONSIDERED | <i>12-6-98</i> |
|----------|----------------------|-----------------|----------------|

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|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643 165)            |

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|                     | AA |                 |      |      |       |           |             |
|                     | AB |                 |      |      |       |           |             |
|                     | AC |                 |      |      |       |           |             |
|                     | AD |                 |      |      |       |           |             |
|                     | AF |                 |      |      |       |           |             |
|                     | AF |                 |      |      |       |           |             |
|                     | AG |                 |      |      |       |           |             |
|                     | AH |                 |      |      |       |           |             |
|                     | AI |                 |      |      |       |           |             |
|                     | AJ |                 |      |      |       |           |             |
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|                     | AL |                 |      |         |       |           | Yes<br>No   |
|                     | AM |                 |      |         |       |           | Yes<br>No   |
|                     | AN |                 |      |         |       |           | Yes<br>No   |
|                     | AO |                 |      |         |       |           | Yes<br>No   |
|                     | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|           |    |   |   |
|-----------|----|---|---|
| <i>AR</i> | AR | 7 | Lao, M-S. et al., "Degradative activities in a recombinant chinese hamster ovary cell culture," <i>Cytotechnology</i> 22:43-52 (December 1996)  |
| <i>AS</i> | AS | 7 | Le Gros, G.S. et al., "The Effects of Sodium Butyrate on Lymphokine Production," <i>Lymphokine Research</i> 4:221-227 (1985)  |
| <i>AT</i> | AT | 7 | Maurer, H.R., "Towards Chemically-defined, Serum-free Media for Mammalian Cell Culture," <i>Animal Cell Culture. a practical approach</i> , R.I. Freshney, ed., IRL Press, Oxford, pp. 13-31 (1986) |

EXAMINER

*Delwin K. Web*

DATE CONSIDERED

12-6-99

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|  |  | APPLICANT<br>Gorfien et al.              |                               |
|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643<br>1651         |

## U.S. PATENT DOCUMENTS

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|                     | AA |                 |      |      |       |           |             |
|                     | AB |                 |      |      |       |           |             |
|                     | AC |                 |      |      |       |           |             |
|                     | AD |                 |      |      |       |           |             |
|                     | AE |                 |      |      |       |           |             |
|                     | AF |                 |      |      |       |           |             |
|                     | AG |                 |      |      |       |           |             |
|                     | AH |                 |      |      |       |           |             |
|                     | AI |                 |      |      |       |           |             |
|                     | AJ |                 |      |      |       |           |             |
|                     | AK |                 |      |      |       |           |             |

## FOREIGN PATENT DOCUMENTS

| EXAMINER<br>INITIAL |    | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
|---------------------|----|-----------------|------|---------|-------|-----------|-------------|
|                     | AL |                 |      |         |       |           | Yes<br>No   |
|                     | AM |                 |      |         |       |           | Yes<br>No   |
|                     | AN |                 |      |         |       |           | Yes<br>No   |
|                     | AO |                 |      |         |       |           | Yes<br>No   |
|                     | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|             |    |   |   |
|-------------|----|---|---|
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| EXAMINER   | <i>John F. Ulrey</i> | DATE CONSIDERED<br><i>12-06-99</i> |
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| EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant. |                      |                                    |

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| FORM PTO-1449<br><u>INFORMATION DISCLOSURE STATEMENT</u> |  | ATTY. DOCKET NO.<br>0942.4110002/RWE/GER | APPLICATION NO.<br>09/028,514 |
|  |  | APPLICANT<br>Gorfien et al.              |                               |
|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643<br>1657         |

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| EXAMINER<br>INITIAL |    | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
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| EXAMINER<br>INITIAL |    | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
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|                     | AN |                 |      |         |       |           | Yes<br>No   |
|                     | AO |                 |      |         |       |           | Yes<br>No   |
|                     | AP |                 |      |         |       |           | Yes<br>No   |

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| EXAMINER | <i>Deborah K. Way</i> | DATE CONSIDERED |
|----------|-----------------------|-----------------|
|          |                       | 12-6-99         |

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| FORM PTO-1449<br><u>INFORMATION DISCLOSURE STATEMENT</u> |  | ATTY. DOCKET NO.<br>0942.4110002/RWE/GER | APPLICATION NO.<br>09/028,514 |
|  |  | APPLICANT<br>Gorfien et al.              |                               |
|  |  | FILING DATE<br>February 23, 1998         | GROUP<br>1643<br><i>165</i>   |

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| AN                       |  |                 |      |         |       |           | Yes<br>No   |
| AO                       |  |                 |      |         |       |           | Yes<br>No   |
| AP                       |  |                 |      |         |       |           | Yes<br>No   |

| OTHER (Including Author, Title, Date, Pertinent Pages, etc.) |    |           |  |   |  |  |  |
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| EXAMINER   | <i>Delphine K. Abou</i> | DATE CONSIDERED | <i>12-6-99</i> |
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|   |  | APPLICANT<br>Gorfien et al.      |                               |
|   |  | FILING DATE<br>February 23, 1998 | GROUP<br>1651                 |
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|                  | AD  |                 |            |                   |       |           |             |
| <i>dku</i>       | AE3 | 4,786,599       | 11/22/1988 | Chessebeuf et al. | 435   | 240.31    | 03/23/1984  |
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| <i>dku</i>       | A13 | 5,393,558       | 02/28/1995 | Allison et al.    | 427   | 126.2     | 06/07/1993  |
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|                  | AL  |                 |            |               | —     | —         | Yes<br>No   |
| <i>dku</i>       | AM2 | GB 901,673      | 07/25/1962 | Great Britain | —     | —         | Yes<br>No   |
| <i>dku</i>       | AN2 | JP 2-49579      | 02/19/1990 | Japan         | —     | —         | Yes<br>X No |
| <i>dku</i>       | AO2 | WO 97/34999     | 09/25/1997 | WIPO          | —     | —         | Yes<br>No   |
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|            |    |           |   |
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| <i>dku</i> | AT | <u>11</u> | Boyce, S.T., and Ham, R.G., "Calcium-Regulated Differentiation of Normal Human Epidermal Keratinocytes in Chemically Defined Clonal Culture and Serum-Free Serial Culture," <i>J. Invest. Dermatol.</i> 81:33S-40S (1983) |

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*Dilukta K. Dku*

DATE CONSIDERED

12-8-99

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|                  | AL              |      |         |       |           | Yes<br>No   |
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|                  | AO              |      |         |       |           | Yes<br>No   |
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| SKC | AT | 12 | Daley, J.P., and Epstein, D.A., "Growth of Human Epidermal Keratinocytes in Keratinocyte Serum-free Medium," <i>Focus</i> 12:68-71 (1990)  |

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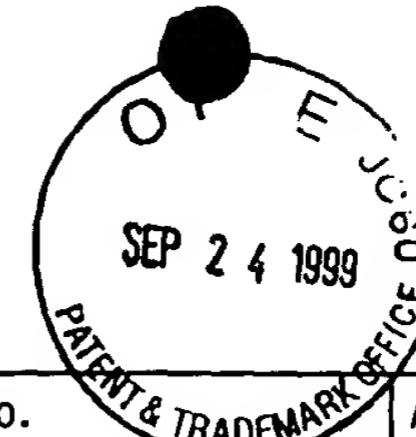
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| AM               |                 |      |         |       |           | Yes<br>No   |
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|   |  | APPLICANT<br>Gorfien et al.      |                               |
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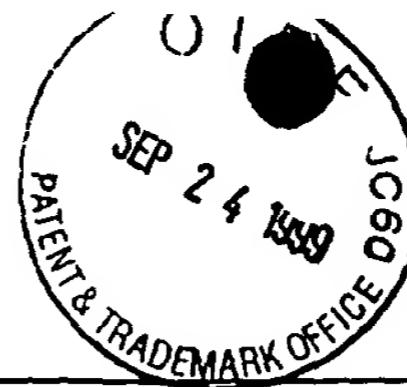
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| AO               |                 |      |         |       |           | Yes<br>No   |
| AP               |                 |      |         |       |           | Yes<br>No   |

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|           |    |           |   |
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| <i>dk</i> | AS | <u>14</u> | Gilchrest, B.A., et al., "Characterization and Partial Purification of Keratinocyte Growth Factor From the Hypothalamus," <i>J. Cell. Physiol.</i> 120:377-383 (1984)   |
| <i>dk</i> | AT | <u>14</u> | Gorfien, S.F., et al., "Recombinant Protein Production by CHO Cells Cultured in a Chemically Defined Medium," poster presented at the Japanese Association for Animal Cell Technology (JAACT), 1996, Yokohama, Japan (September 1996) |

| EXAMINER | DATE CONSIDERED |
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|   |  | APPLICANT<br>Gorfien et al.      |                               |
|   |  | FILING DATE<br>February 23, 1998 | GROUP<br>1651                 |

## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

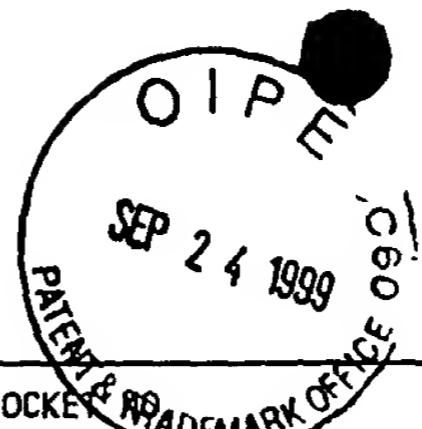
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| AO               |                 |      |         |       |           | Yes<br>No   |
| AP               |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

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| <i>dk</i> | AT | 15 | Keay, L., "Autoclavable Low Cost Serum-Free Cell Culture Media. The Growth of L Cells and BHK Cells on Peptones," <i>Biotechnol. Bioengin.</i> 17:745-764 (1975)  |

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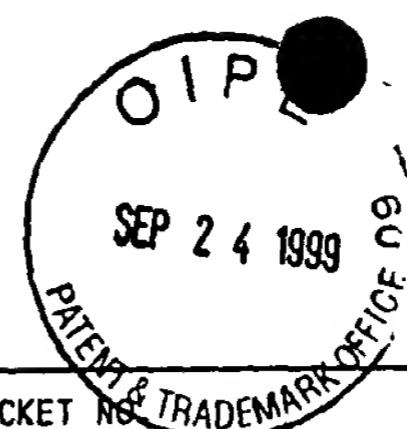
## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|             |    |    |  |
|-------------|----|----|--|
| <i>John</i> | AR | 16 | Konno, Y., et al., "Effect of Zinc on In Vitro Cell Growth Using Serum-Free Culture Media," <i>Cell Struct. Func.</i> 4(4):371 (1979)  |
| <i>John</i> | AS | 16 | Lasfargues, E.Y., et al., "A Serum Substitute That Can Support the Continuous Growth of Mammary Tumor Cells," <i>In Vitro</i> 8:494-500 (1973)                                       |
| <i>John</i> | AT | 16 | Maciag, T., et al., "An endothelial cell growth factor from bovine hypothalamus: Identification and partial characterization," <i>Proc. Natl. Acad. Sci. USA</i> 76:5674-5678 (1979) |

EXAMINER

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| FORM PTO-1449<br><b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</b> |  | ATTY. DOCKET NO. 0942.4110002    | APPLICATION NO. 09/028,514 |  |
|   |  | APPLICANT<br>Gorfien et al.      |                            |  |
|   |  | FILING DATE<br>February 23, 1998 | GROUP<br>1651              |  |

## U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
|------------------|-----------------|------|------|-------|-----------|-------------|
| AA               |                 |      |      |       |           |             |
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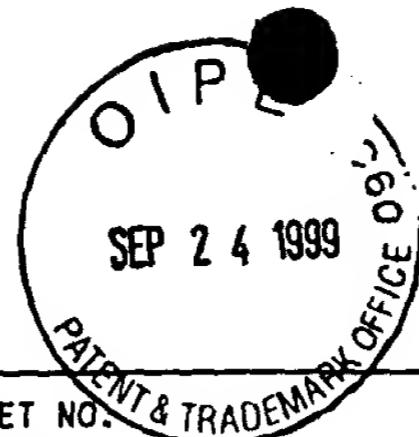
| EXAMINER INITIAL | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
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| AL               |                 |      |         |       |           | Yes<br>No   |
| AM               |                 |      |         |       |           | Yes<br>No   |
| AN               |                 |      |         |       |           | Yes<br>No   |
| AO               |                 |      |         |       |           | Yes<br>No   |
| AP               |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|   |    |    |  |
|---|----|----|--|
|  | AR | 17 | Maciag, T., et al., "An Endocrine Approach to the Control of Epidermal Growth: Serum-Free Cultivation of Human Keratinocytes," <i>Science</i> 211:1452-1454 (1981) |
|   | AS | 17 | Peehl, D.M. and Ham, R.G., "Growth and Differentiation of Human Keratinocytes Without a Feeder Layer or Conditioned Medium," <i>In Vitro</i> 16(6):516-525 (1980)  |
|   | AT | 17 | Pirisi, L., et al., "Transformation of Human Fibroblasts and Keratinocytes with Human Papillomavirus Type 16 DNA," <i>J. Virol.</i> 61:1061-1066 (1987)            |

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| FORM PTO-1449  |  | ATTY. DOCKET NO.<br>0942.4110002 | APPLICATION NO.<br>09/028,514 |
| <u>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</u> |  | APPLICANT<br>Gorfien et al.      |                               |
|  |  | FILING DATE<br>February 23, 1998 | GROUP<br>1651                 |

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|------------------|----|-----------------|------|---------|-------|-----------|-------------|
|                  | AL |                 |      |         |       |           | Yes<br>No   |
|                  | AM |                 |      |         |       |           | Yes<br>No   |
|                  | AN |                 |      |         |       |           | Yes<br>No   |
|                  | AO |                 |      |         |       |           | Yes<br>No   |
|                  | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|           |    |           |   |
|-----------|----|-----------|---|
| <i>AB</i> | AR | <u>18</u> | Pittelkow, M.R., and Scott, R.E., "New Techniques for the In Vitro Culture of Human Skin Keratinocytes and Perspectives on Their Use for Grafting of Patients With Extensive Burns," Mayo Clin. Proc. 61:771-777 (1986)   |
| <i>AS</i> | AS | <u>18</u> | Schlaeger, E.-J., "The protein hydrolysate, Primatone RL, is a cost-effective multiple growth promoter of mammalian cell culture in serum-containing and serum-free media and displays anti-apoptosis properties," J. Immunol. Meth. 194:191-199 (August 1996)  |
| <i>AT</i> | AT | <u>18</u> | Shiloach, J. et al., "Continuous Production of the Extracellular Domain of Recombinant Human Ca <sup>+</sup> Receptor from HEK 293 Cells using Novel Serum Free Medium," in <i>Animal Cell Technology</i> , M. Carrondo, et al., eds., Kluwer Academic Publishers, Netherlands, pp. 535-540 (December 1996) |

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| FORM PTO-1449<br><b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT</b> |  | ATTY. DOCKET NO.<br>0942.4110002 |  | APPLICATION NO.<br>09/028,514 |  |
|   |  | APPLICANT<br>Gorfien et al.      |  |                               |  |
|   |  | FILING DATE<br>February 23, 1998 |  | GROUP<br>1651                 |  |
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|------------------|----|-----------------|------|---------|-------|-----------|-------------|
|                  | AL |                 |      |         |       |           | Yes<br>No   |
|                  | AM |                 |      |         |       |           | Yes<br>No   |
|                  | AN |                 |      |         |       |           | Yes<br>No   |
|                  | AO |                 |      |         |       |           | Yes<br>No   |
|                  | AP |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|            |    |    |  |
|------------|----|----|--|
| <i>dkw</i> | AR | 19 | Shipley, G.D., and Pittelkow, M.R., "Control of Growth and Differentiation In Vitro of Human Keratinocytes Cultured in Serum-free Medium," <i>Arch. Dermatol.</i> 123:1541A-1544A (1987)                   |
| <i>dkw</i> | AS | 19 | Shipley, G.D., et al., "Growth of Normal Human Keratinocytes and Fibroblasts in Serum-Free Medium Is Stimulated by Acidic and Basic Fibroblast Growth Factor," <i>J. Cell. Physiol.</i> 138:511-518 (1989) |
| <i>dkw</i> | AT | 19 | Letter of November 30, 1998 from counsel at Eli Lilly and Company to counsel at Life Technologies, Inc.  |

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| FORM PTO-1449<br><br>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT |  | ATTY. DOCKET NO.<br>0942.411002  | APPLICATION NO.<br>09/028,514 |
|  |  | APPLICANT<br>Gorfien et al.      |                               |
|  |  | FILING DATE<br>February 23, 1998 | GROUP<br>1651                 |

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| AL                  |                 |      |         |       |           | Yes<br>No   |
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|            |    |    |  |
|------------|----|----|--|
| <i>Don</i> | AR | 20 | Stark, D.H., "The Cultivation of Human Kidney Epithelial Cells in Aggregate Culture For the Production of Recombinant Protein C," Ph.D. Thesis, Purdue University (1994)   |
| <i>Don</i> | AS | 20 | Tilkins, M.L., et al., "Recombinant Protein Production by CHO Cells Cultured in Protein-Free and Serum-Free Media," poster presented at the Cell Culture Engineering V Meeting, San Diego, CA (February 1996)  |
| <i>Don</i> | AT | 20 | Valle, M.A., et al., "Evaluation of Porous Microcarriers in Fluidized Bed Reactor for Protein Production by HEK 293 Cells," in <i>New Developments and New Applications in Animal Cell Technology</i> , O.-W. Merten, et al., eds., Kluwer Academic Publishers, Netherlands, pp. 381-384 (July 1998) |

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| FORM PTO-1449<br>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT |  | ATTY. DOCKET NO.<br>0942.4110002 | APPLICATION NO.<br>09/028,514 |
|  |  | APPLICANT<br>Gorfien et al.      |                               |
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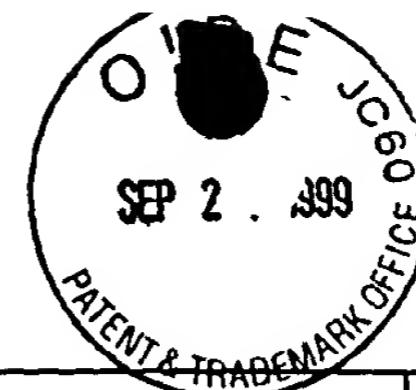
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| AN                  |                 |      |         |       |           | Yes<br>No   |
| AO                  |                 |      |         |       |           | Yes<br>No   |
| AP                  |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|             |    |    |   |
|-------------|----|----|---|
| <i>John</i> | AR | 21 | Wang, J.-W., et al., "Establishment of Three Adenovirus Packaging Cell Lines," <i>Conf. Suppl. Cancer Gene Ther.</i> 3:S24, Abstract No. P-53 (November 1996)   |
| <i>John</i> | AS | 21 | Waymouth, C., "Preparation and Use of Serum-Free Culture Media," in <i>Methods for Preparation of Media, Supplements, and Substrata for Serum-Free Animal Cell Culture</i> , Barnes, D.W., et al., eds., Alan R. Liss, Inc., New York, NY, pp. 23-68 (1984) |
| <i>John</i> | AT | 21 | Wille Jr., J.J., et al., "Integrated Control of Growth and Differentiation of Normal Human Prokeratinocytes Cultured in Serum-Free Medium: Clonal Analyses, Growth Kinetics, and Cell Cycle Studies," <i>J. Cell. Physiol.</i> 121:31-44 (1984)             |

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|   |  | <b>APPLICANT</b><br>Gorfien et al. |                               |
|   |  | FILING DATE<br>February 23, 1998   | GROUP<br>1651                 |

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| AN               |  |                 |      |         |       |           | Yes<br>No   |
| AO               |  |                 |      |         |       |           | Yes<br>No   |
| AP               |  |                 |      |         |       |           | Yes<br>No   |

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

|             |    |           |  |
|-------------|----|-----------|--|
| <i>John</i> | AR | <u>22</u> | Letter from an outside researcher not employed by Life Technologies, Inc. to David Epstein and Dale Gruber                         |
| <i>John</i> | AS | <u>22</u> | Letter from David Epstein and Dale Gruber to an outside researcher not employed by Life Technologies, Inc.                         |
| <i>John</i> | AT | <u>22</u> | Report of experimental results from an outside researcher not employed by Life Technologies, Inc. to David Epstein and Dale Gruber |

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